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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/563,033

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Myriam Fabre

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW

PO BOX 14329

RESEARCH TRIANGLE PARK, NC 27709

EXAMINER

WARE, DEBORAH K

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

11/10/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/563,033	Applicant(s) FABRE ET AL.	
	Examiner DEBBIE K. WARE	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/2/10.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-2 and 4-13 are presented for reconsideration on the merits.

Response to Amendment

The amendment filed August 2, 2010, and Exhibits A and B have been received and entered. The Exhibits were sufficient to remove the objection/rejection over the specification and the claims under 35 USC 112, second paragraph. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0702081 (Publication date: 03/20/1996; as provided by applicant in the 04/17/2006 IDS), hereafter referred to as the Morota publication.

The Morota publication teaches a method for fixing a three-dimensional tissue culture on a sponge in vitro in gelatin solution by elevating the temperature then

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lowering the temperature to coat the culture with 1 to 20 percent (and recites 5 to 10 percent) gelatin (abstract and page 5, lines 40-47). The recitation of a lower limit of 5 percent gelatin anticipates the instantly claimed range (limitation in instant claim 1). The culture is asymmetric in the fact that different cells have been inoculated and cultured on separate layers, the tissues cultures are organized in that they form an organized tissue, and the culture comprises both three-dimensional and two-dimensional cell layers, in that three-dimensional cell layers require a series of two-dimensional cell layers (columns 2-3). The Morota publication recites the gelatin has a sol-gel transition point of 20 to 35° C and recites tissue must be maintained a temperature greater than 10° C and less than 37° C. The working example allows for the gelatin to stand at the lower range of sol-gel transition point (20° C) for 30 minutes (columns 7-8, example 2) and thus anticipates the instantly claimed solidification range and storing temperature range (limitations in instant claims 1 and 6). The cell cultures remain in the gelatin at 20° C for 72 to 120 hours. Further, the Morota publication provides a plate for culture (i.e. a 6-well plate; column 8, fixation by gel), which may be 24- or 6-well plates (column 7, lines 21-25) and the asymmetric support and gelatin solution as noted above, thus providing a kit for the transport and storage of cells (limitations in instant claim 12).

Response to Arguments

Applicant's arguments filed August 2, 2010, have been fully considered but they are not persuasive. Morota et al clearly describe the claimed method wherein gelatin is applied at about 5% and solidifying takes place at 20 deg. Cent. for a period of 3 to 5 days of which 96 hours is equivalent of 4 days. Each of the steps and conditions are

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disclosed, note col. 7, lines 50-60 and col. 8, lines 5-15 and line 14, and lines 20-23.

These claims are anticipated by the teachings of Morota et al. The double-layer structure of dermis cells will inherently have the characteristics of differentiated, polarized and functionally active two-dimensional cell cultures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 to 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1127580 (Publication date: 08/29/2001; as provided by the applicant on the 04/17/2006 IDS), hereafter referred to as the Curatolo publication and EP 0702081 (Publication date: 03/20/1996; as provided by applicant on the 04/17/2006 IDS), hereafter referred to as the Morota publication or WO 01/66783 (Publication date: 09/13/2001; as provided by the applicant on the 04/17/2006 IDS) and EP 0702081

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(Publication date:03/20/1996; as provided by applicant on the 04/17/2006 IDS),
hereafter referred to as the Morota publication.

Applicant claims a method of storing and/or transporting in vitro organized two-dimensional cell cultures by coating the cell culture with gelatin, solidifying the gelatin, and storing and/or transporting the cell culture immobilized in gelatin. The claims further recite liquefaction of the gelatin, elimination of the gelatin, and incubation of the culture in a kit with a support matrix (i.e. "transwell-type").

The Curatolo publication teaches Caco-2 cell monolayers may be cultured on permeable transwell-type supports in media and may be incubated for at least 1 hour at 37° C (paragraph 59) and the Lee publication teaches HUVEC cells cultured in media on gelatin-coated well plates and could be incubated for at least 48 hours (page 20). These monolayers of cells are considered organized, two-dimensional, differentiated, polarized, and functionally active and are considered to be on a support matrix on a well plate (i.e. Curatolo particularly notes "transwell-co filter supports") and as such these cultures are considered to meet the limitations of the support matrix (limitations in instant claims 4, 5, 7, and 10-13).

The Curatolo publication or the Lee publication does not expressly teach method of storing by coating the cell culture support with gelatin, solidifying the gelatin, storing the cells, or liquefying the gelatin. This deficiency in the Curatolo publication or the Lee publication is cured by the teachings of the Morota publication.

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As discussed supra, the Morota publication teaches a method for fixing a three-dimensional tissue culture on a sponge in vitro in gelatin solution by elevating the temperature then lowering the temperature to coat the culture with 1 to 20 percent gelatin. The support is asymmetric and the cultures are organized two- and three-dimensional cultures (limitations in instant claims 1, 6, and 12). Though it would be obvious to optimize the gelatin range (limitations in instant claims 1 and 5), as noted supra the recitation of a lower limit of 5 percent gelatin anticipates the instantly claimed range.

The Morota publication further provides for the removal of the cultures from the gelatin by heating the gelatin to no higher than 37° C to liquefy the gelatin and remove the gelatin from the cultures (column 6, lines 3-18) (limitations in instant claims 2). Though the Morota publication does not recite the time for liquefaction the reversible sol-gel transition process takes 30 minutes to solidify. As one of ordinary skill in the art would want to liquefy the gelatin by heating above 35° C but below 37° C to remove all the gelatin from the cell culture, it would be obvious to heat the cells to this narrow temperature range at a slower rate to control the temperature, prevent heat shock, and maintain cell viability and as such it would be obvious to optimize the liquefaction step to a period of more than 1 hour (limitations in instant claims 8 and 9). The Morota publication has shown that these cells are differentiated and functionally active (column 7, lines 33-49; and column 8, lines 19-54).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare monolayers of Caco-2 cells or HUVEC cells on

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a support matrix as taught as taught by the Curatolo publication or the Lee publication and store or transport the cells by coating the cell culture with gelatin, solidifying the gelatin, storing or transporting the cell cultures, liquefying the gelatin, eliminating the gelatin, and incubating the gelatin as taught by the Morota publication and incubate the cells in media on the support as taught by the Curatolo publication or the Lee publication (limitations in instant claims 1 to 13). One of ordinary skill in the art would have been motivated to do this because the Morota publication teaches the gelatin prevents movement of the safely immobilized culture, protects viable cells during transport, improves workability, and minimizes damage to the culture (column 5, lines 14-23; column 7, lines 39-44; and column 8, lines 41-54).

In light of the forgoing discussion, it would be obvious to one of ordinary skill in the art that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed August 2, 2010, have been fully considered but they are not persuasive. The argument that Morota et al does not cure deficiencies of either Curatolo et al or Lee et al is noted. In response to applicant's argument that the

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references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., defined function at p. 8, lines 1-3 and other examples referred to in their response at page 12, lines 4-5 and reference range of up to 9 days, example 1, p. 12, lines 1-11, example 2: adhesion, migration and invasion assays, and also note p. 7, lines 7-34, and example 1, part 2 for a step requiring getting into functional state prior to coating) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The Morota et al test observed that tissue slice of the model within 96 hours demonstrated that cells had no change with respect to structure and cells were free of separation and damage, note col. 8, lines 29-36. Therefore, the functional state is maintained by the method of Morota et al. Therefore, the fixing method of Morota et al will provide successful results for the Caco-2 cell culture as disclosed by Curatolo and Lee. Applicants claims are not so limited to a particular cell types.

The cells are disclosed by the cited prior art of which it would have been obvious to use the method of Morota et al to carry out the method on these cells because of their recognized dimensionality and desire to store and transport these types of cells in the art. Morota et al do indeed teach in vitro models and methods therefore. The cells are on the device (e.g. transwell support or well plated devices) or model (note col. 8, line 6) and are coated. Applicants' claims do not omit the presence of sponges in their

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method. The rejection is sustained and Applicants claims are not as limited to the specifics argued in their response.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Prior art is cited of record on the previously enclosed PTO-1449/PTO-892 Form(s).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DEBBIE K. WARE whose telephone number is (571)272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah K. Ware/
Deborah K. Ware
Primary Examiner
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